REMARKS

Claims 1-15 are currently pending in the application. Claim 1 is in independent form.

Applicant wishes to express their appreciation for the courtesies extended Applicant's representative, Kenneth I. Kohn, during a telephonic interview conducted on March 16, 2010. Claim 11 has been amended as discussed to change "vaccine" to "immunogenic composition".

The sequence listing filed February 13, 2009, is objected to as introducing new matter in to the disclosure. In response thereto, a corrected sequence listing is included removing that which was considered new matter in SEQ ID NO: 9. Reconsideration of the objection is respectfully requested.

Claims 1-11 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. In response thereto, claim 1 has been amended as suggested in the Office Action to more clearly set forth the subject matter. Markush phrases have been added to the appropriate dependent claims. No new matter has been added. Reconsideration of the rejection is respectfully requested.

Claim 11 stands rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Specifically, the Office Action holds that it is not predictable in the art if Apolipoprotein B-100 mini-peptides would prevent or treat obesity in all species, especially in humans.

In response thereto, Applicant does show immunogenicity of the compounds of the present invention in rats (see page 18, lines 7-21, Figure 16, and Table 2).

Antibody responses to the compounds resulted in the suppression of weight gain in rats. It is well known that experiments are performed in rats and mice that translate directly to humans. Experiments were also performed in dogs with good antibody results and weight gain was also suppressed (see page 20). Therefore, one skilled in the art would expect the compounds to work effectively as a vaccine in humans as well.

Furthermore, WO/2002/20040 (hereinafter Reference 1, enclosed in the Declaration herein) discloses that in the case that a macromolecule such as an antibody has been bound to apolipoprotein B-100 which exists on the surface of LDL, lipase such as lipoprotein lipase cannot hydrolize triglyceride due to the steric hindrance caused by the macromolecule bound to apolipoprotein B-100, and thus the formation of free fatty acid, a major factor for obesity, can be inhibited by means of the antibody which can bind to apolipoprotein B-100 (see page 2, lines 16-24 and page 8, lines 22-30 of Reference 1).

In addition, Reference 1 discloses the mechanism of vaccine comprising apolipoprotein B-100 to prevent or treat obesity by inhibiting accumulation of lipids like cholesterol of free fatty acid in cells. That is, human antibody induced by mimetic peptide binds to the epitope of apolipoprotein B-100 on the surface of LDL, thereby prohibiting LDL from binding specifically to a LDL receptor exposed on the cell surface (see page 9, lines 8-17 of Reference 1).

As such, since Reference 1, which is the previous invention presented by Applicant, already discloses the mechanism of vaccine comprising apolipoprotein B-100 in a human, it is not necessary to disclose the mechanism in the present invention. Furthermore, one skilled in the art would easily understand how the hybrid polypeptide

of the present invention works as a vaccine in humans, thus undue experimentation is not necessary for one skilled in the art to practice the present invention.

In support thereof, the Declaration further includes the following documents to demonstrate how the compounds work as a vaccine in humans and that the vaccine of the present invention provides the same results in humans as shown in animals in the present application.

As seen in Document 1 (Maria Lucia Bonfleur, et al., enclosed in the Declaration) and more specifically on page 24, Table 1 shows that body weight in LDLR knock-out mouse is reduced, compared to WT. In this regard, antibodies induced by the vaccine of the present invention can prohibit LDL from binding specifically to a LDL receptor and result in preventing or treating obesity.

Furthermore, Document 2 (Gerald F. Watts, et al., enclosed in the Declaration) proves the correlation between the reduction of Apolipoprotein B-100 and the suppression of body weight in humans (see page 284, section 5.2). Thus, Documents 1 and 2 combine to show that the results in animals produced by the vaccine of the present invention are predictable of results in humans.

Reconsideration of the rejection is respectfully requested.

Claims 1-11 stand rejected under 35 U.S.C. §103(a) as being unpatentable over WO/2002/20040 to Kim and U.S. Patent No. 6,541,011 to Punnonen. Specifically, the Office Action holds that Kim discloses Apolipoprotein B-100 mini-peptides comprising SEQ ID NO: 1, 2, and 3, which are 100% identical to those of the present invention, and that the peptides can reduce body weight in mice. The Office Action holds that Punnonen discloses a multivalent antigenic polypeptide comprising different epitopes

and an HBV Pre-S peptide that is identical to SEQ ID NOs: 7 and 9 of the present invention. Reconsideration of the rejection under 35 U.S.C. §103(a), as being unpatentable over Kim and Punnonen is respectfully requested.

> "Any need or problem known in the field of endeavor at the time of invention and addressed by the patent can provide a reason for combining the elements in the manner claimed"; however, that reason must be present for the combination to be obvious. *KSR Intern Co. v. Teleflex*, 127 S. Ct. 1727, 1742, U.S. (2007). This requirement was confirmed in *Takeda Chem. Indust., et al. v. Alphapharm*, No. 06-1329 (Fed. Cir. 2007).
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> "The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit." MPEP Section 2143.
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> "The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art." *KSR International Co. v. Teleflex Inc.*, 83 UDPQ2d 1385, 1395 (2007) and MPEP Section 2143.

Kim discloses a mimetic peptide for the epitope of apolipoprotein B-100 which can be used as a vaccine. In this formulation, the active compound can be "mixed or diluted with immune adjuvant" and the immune adjuvant can be proteins containing the epitope of a T cell or T or B cell activators, among other things (p. 6, line 20 – p. 7, line 15). Kim does not disclose an immunogenic hybrid polypeptide, in which the C-terminus of a peptide is fused to the *N*-terminus of a helper T cell epitope as required by the presently amended claims. There is no suggestion or reason in Kim to create such a compound.

While Punnonen discloses an HBV vaccine that can include B or T epitopes from other antigens in the HBsAg sequence, this is a completely different compound from that disclosed in the present invention, and there is no reason to believe that including a T cell epitope in one vaccine means that including one in any vaccine will produce the same results. Furthermore, no evidence is provided in Punnonen that including a T cell epitope actually works. Thus, there is no reason to combine Kim with Punnonen, especially since Kim shows that the vaccine therein is effective.

The present invention provides improved and unexpected results over the disclosure of Kim because of the inclusion of the T cell epitope in the active compound. "When a T cell epitope was fused to a mimetic peptide of the B cell epitope of apo B-100, $PB1_4$ had improved ability to induce antibody responses and displayed vaccine efficacy for an extended period of time, and so had an excellent anti-obesity effect." Specification, p. 7, lines 24-28. The immunogenicity achieved in the examples is due to the inclusion of the T cell epitope along with the B cell epitope. It was shown on pages 19-20 of the specification that a fusion form of the compound with a T cell epitope has higher immunogenicity than the compound itself, such as that disclosed in Kim.

Applicant points out page 22, line 23 to page 23, line 21 of the present application, which describes investigations by the Applicant on the effect of the orientation of the B cell epitope and the helper T cell epitope on the induction of immune response. The Applicant fused a T cell epitope at the N-terminus of an apo-B mimetic peptide, and compared that orientation to the orientation as recited in the invention described by the claims of the present application, namely, a T cell epitope fused at the C-terminus of an apo-B mimetic peptide. The Applicant determined the polypeptide prepared by linking a C-terminus of the apo-B mimetic peptide to a T cell

epitope exhibited a 50-60% enhanced ability to induce antibody response (see Figure 16), and to suppress body weigh gain (see Table 2), as compared to the polypeptide prepared by linking an N-terminus of the apo-B mimetic peptide to a T cell epitope. Thus, the results indicate that a polypeptide prepared by linking a C-terminus of the apo-B mimetic peptide to a T cell epitope as recited in the claims of the present invention has much stronger immunogenicity and anti-obesity effects. However, neither Kim nor Punnonen disclose or suggest these unexpected results, and it would not be obvious for one skilled in the art to make the present invention.

Since neither the cited references alone or in combination with knowledge in the art suggest the currently claimed invention, it is consequently respectfully submitted that the claims are clearly patentable over the combination, even if the combination were to be applied in opposition to applicable law, and reconsideration of the rejection is respectfully requested.

The claims of this application have further been rejected as unpatentable based on provisional non-statutory obviousness-type double patenting over U.S. Patent No. 6,825,318. As noted in the Office Action, these rejections can be readily overcome by the filing of a terminal disclaimer in compliance with 37 C.F.R. 1.321(c) or (d). Applicant herein provides the appropriate terminal disclaimer.

The remaining dependent claims not specifically discussed herein are ultimately dependent upon the independent claims. References as applied against these dependent claims do not make up for the deficiencies of those references as discussed above, and the prior art references do not disclose the characterizing features of the independent claims discussed above. Hence, it is respectfully submitted that all of the pending claims are patentable over the prior art.

In view of the present amendment and foregoing remarks, reconsideration of the rejections and advancement of the case to issue are respectfully requested.

The Commissioner is authorized to charge any fee or credit any overpayment in connection with this communication to our Deposit Account No. 11-1449.

Respectfully submitted,

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CERTIFICATE OF ELECTRONIC FILING VIA EFS-WEB

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I hereby certify that this correspondence is being electronically filed with the United States Patent & Trademark Office on the above date.

/Natalie Zemgulis/
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